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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,587	04/03/2001	Lorraine D. Butlin	IMIN.P-032	8700

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EXAMINER	
NGUYEN, BAO THUY L	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,587	BUTLIN ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 01/11/04 has been received. Claims 1-20 and 51-54 have been canceled. Claims 21-50 are pending.

Rejection Withdrawn

2. The rejection of claims 21-23, 29, 35-38 and 44-47 under 35 U.S.C. 102) as being anticipated by Shah et al (US 4,900,662) is withdrawn in view of Applicant's arguments.

3. The rejection of claims 24-28, 30-34 and 39-43 under 35 U.S.C. 103(a) as being unpatentable over Shah et al in view of Creus et al is withdrawn in view of Applicant's arguments.

New Rejections

Claim Rejections - 35 USC § 112, Second paragraph

4. Claims 21-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is confusing because it is unclear what is being claimed. The claim appears to be drawn to a method for diffentiating between two different states of an analyte that exists in a plurality of different forms, i.e. a method for detecting different isoforms of an analyte. However, the preamble claim 21 also states that the first state of the analyte differs from the second state of the analyte because it contains the different forms of the analyte in different amounts. Therefore, it is unclear if applicant is claiming a method for differentiating between at least two different isoforms of an analyte, or if two different states of an analyte are

differentiated by detecting the amount of the same analyte at different time intervals of in different samples.

Claim 21 is also confusing because there is no clear correlation between the preamble of the claim and what is being detected. Claim 21 recites that the amount of the first binding agent/analyte/second binding agent complex formed in the first and second assays differs depending on the state of the analyte in the sample. Where is the differentiating? Does the amount of the complex in certain ranges determine that state or form the analyte is in? In other words, how would one know which form the analyte is in based on the amount detected?

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 48-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to provide an adequate written description of the invention and fails to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR 1.801-1.809.

The specification lacks complete deposit information for the hybridoma cell lines known as ECACC 00032004 and ECACC 00032005. Without a publicly available deposit of the above cell lines, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Applicants must comply with the criteria set forth in 37 CFR 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty, that the cell lines will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the cell lines will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
- the deposits were viable at the time of deposit; and,
- that the deposits will be replaced if they should ever become non-viable.

In the instant case, there is not available a viability statement, i.e. one certifying that the deposit was viable at the time of the deposit or a certificate verifying such from the depository, nor is there a statement that the cell lines will be irrevocably and without restriction or

condition released to the public upon the issuance of a patent and that the cell lines will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit along with the necessary statements in order to meet the criteria se forth in 37 CFR 1.801-1.809.

7. Claims 21-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are drawn to a method for diffentiating between two different states of an analyte that exists in a plurality of different forms. According to the preamble of the claim, the first state differs from the second state because it contains the different forms of the analyte in different amounts. As discussed above, this claim is confusing because it is unclear how the different forms of the analyte are differentiated. Furthermore, the claims and arguments

submitted on 11 January 2004 states that the binding reagents are the same in each assay (i.e. the first binding reagent in step b is the same as the first binding agent in step c; and the second binding agent in step b is the same as the second binding agent in step c) but different from one another (i.e. the first binding agent is different from the second binding agent); if such is the case, how does one differentiate between different isoforms or different amount of the isoforms? Because the reagents in each assay are the same, presumably they would bind to the same analyte, and may cross react with different isoforms of the same analyte; however, because only the end result is observed (i.e. the labeling effect of the second binding reagent), how does one detect whether it is isoform A or isoform B, for example, that is bound by the binding reagent. There is nothing in the claims that would lead one to the conclusion that in the first assay, only isoform A detected and in the second assay, only isoform B is detected, or vice versa. In the other scenario, the claim also does not lead one to the conclusion that if X amount of an analyte is detected in the first assay, that such amount means isoform A is present in the sample, or if Y amount of analyte is detected in the first assay, that such an amount means isoform B is present in the sample.

Nothing in the specification teaches one how to distinguish between the different isoforms of the analyte based on their amount in a sample; nor is there a teaching that the different isoforms of the analyte can be differentiated using the method of the invention. The claims and Example 3 of the specification appear to be a method for detecting the same analyte using contemporaneous samples from the same source. The specification teaches that FSH concentration in each sample was measured by the two-step and one-step assays and the ratio obtained are expressed as a single number. The specification does not teach that the one-step

and two-step assays are able to distinguished between two different isoforms of FSH in either aliquots of a single sample or contemporaneous samples from the same source.

While it is true that every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in this specification with respect to a method for differentiating between a first state and second state of analyte by performing a one-step and a two-step assay on contemporaneous samples from the same source or aliquots of a single sample using the same first binding partner and second binding partner in each of the assay. The binding partners are different from each other.

Since the specification fails to teach those in the art how to make and use the invention without undue experimentation, it is maintained that the claims are not enabled by the specification.

8. Claims 21-50 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for distinguishing between pre-menopausal and post-menopausal FSH in samples at different time intervals, does not reasonably provide enablement for a method for differentiating between a first state and a second state of an analyte (i.e. FSH) in contemporaneous samples using the same reagents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification page 9, lines 6-10 teaches the analysis of FSH samples using a pair of novel anti-FSH monoclonal antibodies that distinguish between pre-menopausal and post-

menopausal FSH samples. The specification further teaches that for more accurate diagnosis of menopausal conditions the assay results should be determined numerically, and expressed as a ratio of the signals of the first and second assays. A significant change in this ratio can indicate transition from a pre-menopausal to a post-menopausal state, or vice-versa. Thus the results from a series of contemporaneous tests performed, for example, every few weeks, can be collated and any change in the observed signal ratio used to diagnose a change in condition. Page 11, lines 5-19.

The specification does not teach the method as claim in claim 21, mainly the performance of a one-step and two-step assays on contemporaneous samples from the same source, and the comparison of the amount of analyte detected in the one-step assay and the two-step assay, where the amount of analyte found in these assays is used to differentiate between two different states of the analyte.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 9:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641